

## Organic Chemistry II

### Summary of Substituent Effects

Substituents bonded to a benzene ring can influence the electronic characteristics of the ring by either donating electrons (electron-donating groups (EDG); increase negative character) or withdrawing electrons (electron-withdrawing groups (EWG); increase positive character) from the ring. Substituents can donate or withdraw electrons from the ring through *resonance effects* or *inductive effects*. There are a number of *different* reactions involving substituted benzene rings where substituents influence the reaction through substituent effects. In order to understand the significance of a substituent effect, the specific mechanism of each reaction must be evaluated to determine exactly how a substituent influences the reaction.

Sigma ( $\sigma$ ) values are experimental values that are assigned to substituents that take into account both a substituent's resonance and inductive effects. The sigma value has a sign (+ or -) and a magnitude or numerical value. The sign of the sigma value indicates whether the substituent is an EDG or EWG. *Substituents with a + sigma value are EWG and substituents with a negative sigma value are EDG.* Substituents with a larger magnitude (absolute value) have greater electron-donating (if negative) or electron-withdrawing (if positive) character.

Electrophilic Aromatic Substitution (EAS): In the EAS reaction, one of the pi bonds of the ring reacts with an electrophile (E+). The ring serves as the nucleophilic (negative) species in the EAS reaction. The rate of the reaction is enhanced if the nucleophilic species, i.e., the ring, is more negative. *Substituents that increase the negative character of the ring (EDG) increase the rate of the EAS reaction. Substituents that decrease the negative character (or increase the positive character, EWG) of the ring decrease the rate of the reaction.* Generally, sigma values\* are NOT used for EAS reactions but the EDG or EWG character of substituents are determined as follows:

- Resonance effects predominate for all substituents EXCEPT halogens. Inductive effects predominate for halogens.
- EDG (by resonance) are identified as those where the atom (usually sp<sup>3</sup> hybridized) directly bonded to the benzene ring has at least one lone pair available to donate into the ring via resonance. These groups are ortho-/para directors
- EWG (by resonance) are identified as those where the atom (usually sp<sup>2</sup> hybridized) directly bonded to the benzene ring is part of an external pi system where electrons from the pi bond of the benzene ring can delocalize out of the ring (i.e., be withdrawn) These groups are meta directors.
- EWG (by induction) are halogens. Halogens are in a class by themselves as substituents. These groups withdraw electrons through an inductive effect because they are so electronegative. The resonance effects associated with halogens are weaker but they do predict the directing ability of halogens. These groups are ortho/para directors.

*\*(Sigma values may be used in some cases. When sigma values are used, the para sigma value should be selected from the table)*

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#### Acid/Base Reactions

For all acid base reactions, substituent effects are evaluated in relation to the charged species (i.e, conjugate base for acidic compounds and conjugate acid for basic compounds) in the ionization process. The effect of the substituent on the conjugate acid or base influences the  $K_a$  (equilibrium constant) of the ionization, which in turn influences the  $pK_a$  or acid strength. For basic compounds, the acid strength of the conjugate acid can then be related to the  $pK_b$ , or base strength. (Note: Always draw the ionization scheme to express  $K_a$  with the acid on the left and the base on the right).

For acidic functional groups:

$$K_a = \frac{[\text{conjugate base}]}{[\text{acid}]}$$

For basic functional groups:

$$K_a = \frac{[\text{base}]}{[\text{conjugate acid}]}$$

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$$pK_a = -\log K_a$$

$$pK_a + pK_b = 14$$

*Sigma values are used to determine the electron-donating or electron-withdrawing characteristics of a particular substituent in acid/base reactions.* When the substituent is either para or ortho to the ionizable functional group (benzoic acid, phenol, sulfonamide, aniline), the para sigma value is used. When the substituent is meta to the ionizable functional group, the meta value is used.

**pKa of Benzoic Acids, Phenols, and Sulfonamides (acidic):** Ionization of acids results in the generation of a negatively charged conjugate base. Increasing the negative character (EDG) of the benzene ring of the acid destabilizes the negative charge on the conjugate base. Increasing the positive character (EWG) of the benzene ring stabilizes the negative charge on the conjugate base. When the conjugate base is stabilized, the concentration of the conjugate base increases, the  $K_a$  of the ionization process increases, and the  $pK_a$  of the acid is lowered (stronger acid)

**pKa of Anilines (basic):** The conjugate acid of anilines is positively charged. Increasing the negative character (EDG) of the benzene ring of the aniline stabilizes the positive charge on the aniline's conjugate acid. Increasing the positive character (EWG) of the benzene ring destabilizes the positive charge on the conjugate acid. When the conjugate acid is stabilized, the concentration of the conjugate acid increases, the  $K_a$  of the ionization process decreases, and the  $pK_a$  of the acid is raised (weaker conjugate acid). A higher  $pK_a$  for the conjugate acid means a lower  $pK_a$  for the base (stronger base).

#### Electrophilic Addition of Substituted Styrenes

Substituents on the benzene ring can stabilize or destabilize the carbocation that is generated in the rate-determining step of the electrophilic addition reaction of styrenes. Since the carbocation is positively charged, EDG stabilize the carbocation and lower its energy. Lowering the energy of the carbocation also lowers the energy of the transition state and decreases the overall activation energy of the rate-determining step of the reaction and the overall reaction, making the reaction FASTER. EWG destabilize the carbocation by making the ring positive. This results in raising the energy of the carbocation, its transition state and the activation energy and the reaction rate is slowed down.

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Base-Catalyzed Hydrolysis of Benzoate Esters

Substituents on the benzene ring can stabilize or destabilize the tetrahedral intermediate that is generated in the rate-determining step of the base-catalyzed hydrolysis of benzoate esters. Since the tetrahedral intermediate is negatively charged, EDG destabilize the tetrahedral intermediate and raise its energy. Raising the energy of the tetrahedral intermediate also raises the energy of the transition state and increases the overall activation energy of the rate-determining step of the reaction and the overall reaction, resulting in a SLOWER reaction. EWG stabilize the tetrahedral intermediate by making the ring positive. This results in lowering the energy of the tetrahedral intermediate, its transition state and the activation energy and the reaction rate is FASTER.

The table below summarizes substituent effects for the reactions described above.

Reaction	What is the substituent influencing?	Sigma Value used?	What does EDG do?	What does EWG do?
Electrophilic Aromatic Substitution (EAS)	Substituents make ring more or less negative for reaction with electrophile	Not usually but can use $\sigma$ para values	increase the negative character of the ring and increase the rate of the reaction (ACTIVATORS)	decrease the negative character of the ring (increase positive) and decrease the rate of reaction (DEACTIVATORS)
pKa of Benzoic Acids, Phenols, and Sulfonamides	Substituents stabilize or destabilize the negatively charged conjugate base ⊖	Yes.	increase the negative character of the ring and destabilize the conjugate base RAISES pKa ⊖	increase the positive character of the ring and stabilize the conjugate base LOWERS pKa ⊕
pKa of Anilines	Substituents stabilize or destabilize the positively charged conjugate acid ⊕	Yes	increase the negative character of the ring and stabilize the conjugate acid RAISES pKa, LOWERS pKb ⊖	increase the positive character of the ring and destabilize the conjugate acid LOWERS pKa; RAISES pKb ⊕
Electrophilic Addition of Styrenes	Substituents stabilize or destabilize the carbocation formed in the rate-determining step ⊕	Yes	increase the negative character of the ring and stabilize the carbocation FASTER RATE ⊖	increase the positive character of the ring and destabilize the carbocation SLOWER RATE ⊕
Base-Catalyzed Hydrolysis of Benzoate Esters	Substituents stabilize or destabilize the tetrahedral intermediate formed in the rate-determining step ⊖	Yes	increase the negative character of the ring and destabilize the tetrahedral intermediate SLOWER RATE ⊖	increase the positive character of the ring and stabilize the tetrahedral intermediate FASTER RATE ⊕